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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/051,663	01/18/2002	Vernon M. Ingram	M00656/70071 (JRV)	3098

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EXAMINER	
CELSA, BENNETT M	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 04/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/051,663	INGRAM ET AL.	
	Examiner	Art Unit	
	Bennett Celsa	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7,8,10,12-16,22,24,26-29 and 31-41* is/are pending in the application.

4a) Of the above claim(s) *1,7,8,10,12-16,22,24,26-28 and 31-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/20/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION: Substitute Office Action

Status of the Claims

Claims 1, 7, 8, 10, 12-16, 22, 24, 26-29 and 31-41 are currently pending.

Claim 29 is under consideration.

Claims 1, 7, 8, 10, 12-16, 22, 24, 26-28 and 31-41 are withdrawn from consideration as being directed to a nonelected invention.

NOTE: THE FOLLOWING OFFICE ACTION REPLACES THE PREVIOUS EXAMINER OFFICE ACTION MAILED JANUARY 13, 2004 (1/13/04)

Election/Restriction

1. Applicant's election with traverse of Group V (claim 29: composition comprising an inhibitor of neural membrane depolarization and a compound that decrease neuronal calcium influx), with traverse, in applicant's response dated 10/31/03 is acknowledged. The traversal is on the ground(s) that Group XIII (claim 38) recites the use of the composition of claim 33 which would not require additional search burden since a search of the elected composition would find art related to its use. This is not found persuasive since a search of the composition is not limited to a single use and the additional search of claim 38 is burdensome for the reasons provided in the reasons for restriction (e.g. different and separate manual/computer bibliographic and classification search of patent and literature). In this regard, it is noted that in accordance with U.S. practice, upon the allowance of a compound claim within an elected compound invention , the Examiner will *consider rejoinder of* a method of use

which is commensurate in scope to the allowed subject matter pursuant to MPEP 821.04 Rejoinder. The requirement is still deemed proper and is therefore made FINAL.

2. Applicant's election of *tyrosine kinase inhibitors* and the compound DAPH1 (4,5-dianilinophtalimide) as a compound tyrosine kinase species that neuronal membrane depolarization in applicant's response dated 10/31/03 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. In response to the Office Action dated December 15, 2003 (bonafide response letter) Applicant's further correspondence dated January 15, 2004 further electing 2,3-dihydroxy-nitro-7-sulfamoyl-benzo[f]quinoxaline (NBQX) as the compound that decreases neuronal calcium influx is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

4. Claims 1, 7, 8, 10, 12-16, 22, 24, 26-28 and 31-41 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

Specification

Information Disclosure Statement

5. The disclosure is objected to because of the following informalities: The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the Examiner on form PTO-892, they have not been considered.

6. Claim 29 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (lack of written description).

It is first noted that written description is legally distinct from enablement: "Although the two concepts of are entwined, they are distinct and each is evaluated under separate legal criteria. The written description requirement, a question of fact, ensures the that the inventor conveys to others that he or she had possession of the claimed invention; whereas, the enablement requirement, a question of law, ensures that the inventor conveys to others how to make and use the claimed invention." See 1242 OG 169 (January 30, 2001) citing *University of California v. Eli Lilly & Co*

With regard to the description requirement, Applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.,* 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original)[The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)].

The *Lilly* court sets forth a two part test for written description: A description of a genus of cDNA's may be achieved by means of a recitation of:

1. a representative number of cDNA's, defined by nucleotide sequence, falling within the scope of the genus Or

2. of a recitation of structural features common to the members of the genus.

See *Regents of the University of California v. Eli Lilly & Co.* 119 F.3d 1559 (Fed. Cir. 1997) at 1569.

The present claim is directed to:

A composition comprising:

a. one or more *"compounds that decrease membrane depolarization of neuronal cells"* (e.g. *tyrosine kinase inhibitors)* caused by aggregated beta-amyloid (Abeta) protein degradation products, and

b. one or more compounds that *"decrease neuronal calcium influx by beta amyloid protein degradation products"*.

In support thereof, the specification merely provides a handful of compounds corresponding to item a.(e.g. various functional categories of compounds (e.g. tyrosine kinase inhibitors etc.) And item b. (e.g. Non-NMDA channel antagonist compounds, decoy peptides) in which functional/mechanistic properties are not correlative to a single compound core structure. See e.g. Ingram et al. PG PUB US 2003/0114510A1 (6/03) (of present application) at pages 1-7.

In the present instance, neither the specification nor the claims provide:

1. A recitation of structural features common to the members of the " genera" corresponding

to *"compounds that decrease membrane depolarization of neuronal cells"* or *"compounds that decrease neuronal calcium influx by beta amyloid protein degradation products" OR*

2. a representative number of inhibitors of depolarization of neuronal cell membranes or a representative number of compounds that decrease neuronal calcium influx.

Accordingly, neither the specification nor claims demonstrate possession of the presently claimed function/mechanistic claimed generics.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Buxbaum Pat No. 5,385,915 (1/95) alone or further in view of Ingram et al. PG PUB US 2003/0114510A1 (6/03) as evidence of inherency.

The present claim is directed to: A composition comprising:

1. one or more *"compounds that decrease membrane depolarization of neuronal cells"* (e.g. *tyrosine kinase inhibitors)* caused by aggregated beta-amyloid (Abeta) protein degradation products, and

2. compounds that *"decrease neuronal calcium influx by beta amyloid protein degradation products".*

Buxbaum teaches the making of composition comprising:

1. one or more kinase inhibitors (e.g. tyrphostin) (e.g. see abstract; see col. 11, line 50; patent claims, especially claims 1, 2, 7, 17 etc.) And

2. one or more calcium modulators (e.g. glutamate) (e.g. see abstract; col. 11, lines 50-61, patent claims, especially claims 1, 8, 10, 20, 30 etc.)

for treating diseases associated with amyloid plaque deposition, especially Alzheimer's disease.

Ingram et al. PG PUB discloses:

that (tyrosine) kinase inhibitors, include tyrphostin compounds, which inherently act to "decrease membrane depolarization" (e.g. see page 1, col. 2, paragraphs [0011-0015])

and

that "compounds that decrease neuronal calcium influx by beta amyloid protein degradation products" include non-NMDA channel antagonists" including "glutamate").

Accordingly, the Buxbaum reference provides explicit motivation for one of ordinary skill in the art to make (e.g. in its disclosure and patent claims) compositions comprising :

1. one or more *"compounds that decrease membrane depolarization of neuronal cells"* (e.g. *tyrosine kinase inhibitors)* caused by aggregated beta-amyloid (Abeta) protein degradation products, and

2. compounds that *"decrease neuronal calcium influx by beta amyloid protein degradation products"*

in order to produce compositions for treating diseases associated with amyloid plaque formation (e.g. Alzheimer's disease).

Accordingly, it would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to make compositions comprising one or more kinase inhibitors (e.g tyrphostin) and one or more calcium modualtors (e.g. glutamate) for treating diseases associated with amyloid plaque aggregation (e.g. Alzheimer's disease) in light of the Buxbaum reference teaching.

9. Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Buxbaum in view of Ingram et al. as applied to claim 29 above, and further in view of Sharpe et al. US Pat. No. 6,552,066 (4/03: filed 9/96 or earlier).

The Buxbaum reference teaching as discussed in the rejection of claim 29 over Buxbaum Pat No. 5,385,915 (1/95) alone or further in view of Ingram et al. PG PUB US 2003/0114510A1 (6/03) as evidence of inherency is hereby incorporated by reference in its entirety.

Buxbaum teaches the making of composition comprising:

1. one or more kinase inhibitors (e.g. tyrphostin) (e.g. see abstract; see col. 11, line 50; patent claims, especially claims 1, 2, 7, 17 etc.) And

2. one or more calcium modulators (e.g. glutamate) (e.g. see abstract; col. 11, lines 50-61, patent claims, especially claims 1, 8, 10, 20, 30 etc.)

for treating diseases associated with amyloid plaque deposition, especially Alzheimer's disease.

To the extent that the Buxbaum reference fails to **explicitly** disclose the selection of DAPH1 (4,5-dianilinophtalimide) as a compound tyrosine kinase species, the Sharpe et al. reference is cited.

The Sharpe reference teaches that **DAPH1** is a member of the Tyrosine kinase family of inhibitors, as disclosed in the Buxbaum reference, including tyrphostin and thus are expected to be functionally equivalent. E.g. see Sharpe at col. 2, lines 15-32-col. 4)..

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to utilize DAPH1 as a kinase inhibiting compound in the Buxbaum reference composition since the Buxbaum reference discloses the use of various kinase inhibiting compounds in its compositions which would include DAPH1 which is taught by the Sharpe reference to be a functionally equivalent member of the tyrosine kinase family of inhibitors which include similar functionally equivalent members (e.g. tyrphostin) as those disclosed in Buxbaum.

10. Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Buxbaum Pat No. 5,385,915 (1/95) alone or further in view of Ingram et al. PG PUB US 2003/0114510A1 (6/03) as evidence of inherency as applied to claim 29 above, and further in view of Ingram WO 98/30229 (7/98) .

The Buxbaum reference teaching as discussed in the rejection of claim 29 over Buxbaum Pat No. 5,385,915 (1/95) alone or further in view of Ingram et al. PG PUB US 2003/0114510A1 (6/03) as evidence of inherency is hereby incorporated by reference in its entirety.

To the extent that the Buxbaum reference fails to **explicitly** disclose the incorporation in its compositions of compounds that *"decrease neuronal calcium influx by beta amyloid protein degradation products"*, which include "decoy peptides" or "non-NMDA channel antagonists", the Ingram WO 98/30229 document is cited.

Ingram WO 98/30229 teaches compositions comprising compounds that *"decrease neuronal calcium influx by beta amyloid protein degradation products" (e.g.*

"decoy peptides" : i.e.. see pages 4, 10-11, 14-15; and "Non-NMDA channel antagonists: see pages 17-18, especially page 17, lines 11-28 which include **NBQX**: see also examples and claims) for treating conditions characterized by unwanted beta-amyloid peptide aggregate formation including Alzheimer's disease. The

Accordingly, one of ordinary skill in the art would have been motivated to incorporate in the Buxbaum reference compositions the Ingram WO 98 "decoy peptide" or Non-NMDA antagonist compounds that *"decrease neuronal calcium influx by beta amyloid protein degradation products"* since:

a. Buxbaum reference teaches the incorporation of calcium channel modulating compounds (e.g. see patent claims, especially claim 10, 26, 30 etc. and "glutamate" ; and

b. The Buxbaum rand Ingram WO 98 reference compositions are made for the same purpose e.g. the treatment of diseases (e.g. Alzheimer's disease) associated with amyloid plaque aggregation.

See also *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980) wherein the court held that it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose.

Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to incorporate into the Buxbaum reference composition compounds that *"decrease neuronal calcium influx by beta amyloid protein degradation products"*, which include "decoy peptides" or Non-NMDA calcium channel antagonists

as taught by Ingram WO 98 with a reasonable expectation of achieving compositions within the scope of the presently claimed invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bennett Celsa whose telephone number is 571-272-0807. The examiner can normally be reached on 8-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-273-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bennett Celsa
Primary Examiner
Art Unit 1639

BC
April 6, 2004